

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
20 March 2003 (20.03.2003)

PCT

(10) International Publication Number
WO 03/022208 A3

- (51) International Patent Classification⁷: **A61K 38/28**, (74) Agent: MYERS BIGEL SIBLEY & SAJOVEC; PO Box 37428, Raleigh, NC 27627 (US).
C07K 14/62
- (21) International Application Number: PCT/US02/28429
- (22) International Filing Date:
6 September 2002 (06.09.2002)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/318,193 7 September 2001 (07.09.2001) US
60/377,865 3 May 2002 (03.05.2002) US
- (71) Applicant (for all designated States except US): **NOBEX CORPORATION** [US/US]; Post Office Box 13940, Research Triangle Park, NC 27709-3940 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **SOLTERO, Richard** [US/US]; 5509 Solomon's Seal Court, Holly Springs, NC 27540 (US). **RADHAKRISHNAN, Balasingham** [US/US]; 209 Faison Road, Chapel Hill, NC 27517 (US). **EKWURIBE, Nnochiri, N.** [NG/US]; 216 Coltsgate Dr., Cary, NC 27511 (US). **REHLAENDER, Bruce** [US/US]; 604 Highgrove Drive, Chapel Hill, NC 27516 (US). **HICKEY, Anthony** [GB/US]; 1208 Killington Court, Chapel Hill, NC 27517 (US). **BOVET, Li, Li** [US/US]; 110 Marin Drive, Chapel Hill, NC 27516 (US).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:
— with international search report
- (88) Date of publication of the international search report:
25 September 2003
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.



WO 03/022208 A3

(54) Title: PHARMACEUTICAL COMPOSITIONS OF INSULIN DRUG-OLIGOMER CONJUGATES AND METHODS OF TREATING DISEASES THEREWITH

(57) Abstract: Pharmaceutical compositions that include an insulin drug-oligomer conjugate, a fatty acid component, and a bile salt component are described. The insulin drug is covalently coupled to an oligomeric moiety. The fatty acid component and the bile salt component are present in a weight-to-weight ratio of between 1:5 and 5:1. Methods of treating an insulin deficiency in a subject in need of such treatment using such pharmaceutical compositions are also provided, as are methods of providing such pharmaceutical compositions.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/28429

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 38/28; C07K 14/62

US CL : 514/3; 530/303

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/3, 4; 530/303, 304, 305

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4,156,719 A (SEZAKI ET AL) 29 May 1979 (29/05/79), see entire document, especially the Abstract, Experiment 1.	51-53
Y		1-50
X,P	US 2002/0018811 A1 (PENTEADO ET AL) 14 February 2002 (14/02/02), see entire document, especially paragraph 98.	51
A	JP 52057313 A (YAMANOUCHI PHARM CO LTD) 11 May 1977 (11/05/77), see entire document.	1-53
Y	WO 00/078302 A1 (PROTEIN DELIVERY, INC.) 28 December 2000 (28/12/00), see entire document, especially page 8, line 6 - page 11, line 26, page 38, line 1 - page 39, line 18.	1-50

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"Z" document member of the same patent family

Date of the actual completion of the international search

02 October 2002 (02.10.2002)

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. (703)305-3230

Date of mailing of the international search report

14 MAR 2003

Authorized officer

Jeffrey E. Russel

Telephone No. (703)308-0196

INTERNATIONAL SEARCH REPORT

PCT/US02/28429

Continuation of B. FIELDS SEARCHED Item 3:

EAST, DIALOG

search terms: insulin, conjugate, fatty acid, oleic, capric, lauric, bile, cholic, cholate, deoxycholate

THIS PAGE BLANK (USPTO)